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EXAMINER	
GIBBS, TERRA C	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/633,843	BENNETT ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/13/04 & 8/4/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a response to Applicant's preliminary amendment filed December 18, 2003.

Claims 3 and 16-20 have been canceled. Claim 1 has been amended. Claims 1, 2, and 4-15 are pending in the instant application.

Claims 1, 2, and 4-15 have been examined on the merits.

Information Disclosure Statement

Applicant's information disclosure statements filed December 13, 2004 and August 4, 2003 are acknowledged. The references referred to therein have been considered on the merits.

Priority

It is noted that this application is a continuation of USSN 09/888,360 filed June 21, 2001, which is now abandoned.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the

best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 11 is drawn to a compound 8 to 50 nucleobases in length which specifically hybridizes with at least an 8-nucleobases portion of an active site on a nucleic acid molecule encoding human superoxide dismutase 1 soluble.

The specification discloses several dozen antisense oligonucleotides directed to human superoxide dismutase 1 soluble, GenBank Accession NO: X02317 (represented as SEQ ID NO:3 in the instant invention) which, although sufficient to adequately describe antisense compounds directed to the human superoxide dismutase 1 soluble (SEQ ID NO:3), do not describe compounds from any other superoxide dismutase 1 soluble gene. The art teaches human superoxide dismutase 1 soluble genes with different GenBank Accession Numbers. For example, the art teaches human superoxide dismutase 1 soluble sequences from GenBank Accession Numbers: NM_000454; AY891823; AY891822; AU889333; AY889332; AY893554; AY835629; CR450355; L44135; AY049787; and M13267, for example. There is no disclosure found in the specification or known in the art that relates the structure of a compound which specifically hybridizes with at least an 8-nucleobases portion of an active site on a

nucleic acid molecule encoding human superoxide dismutase 1 soluble, other than SEQ ID NO:3.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

MPEP 2163 states in part, "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

With the exception of compounds which specifically hybridize with at least an 8-

nucleobases portion of an active site on a nucleic acid molecule encoding human superoxide dismutase 1 soluble, SEQ ID NO:3, the skilled artisan cannot envision the detailed structure of the encompassed compounds, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only compounds which specifically hybridizes with at least an 8-nucleobases portion of an active site on a nucleic acid molecule encoding human superoxide dismutase 1 soluble directed to SEQ ID NO:3, but not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115).

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of *in vitro* (cell culture) inhibition of superoxide dismutase 1 soluble in cells or tissues comprising administering an

antisense compound targeted to the coding region of a nucleic acid molecule encoding superoxide dismutase 1 soluble, does not reasonably provide enablement for *in vivo* (whole organism) inhibition of superoxide dismutase 1 soluble in cells or tissues comprising administering an antisense compound targeted to a coding region of a nucleic acid molecule encoding superoxide dismutase 1 soluble. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This is a scope enablement rejection.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention, and the quantity of experimentation necessary.

Claim 15 is drawn to a method of inhibiting the expression of superoxide dismutase 1 soluble in any cell or tissue comprising administering an antisense compound targeted to the coding region of a nucleic acid molecule encoding superoxide dismutase 1 soluble. The broadness of the method recited in claim 15 implies *in vivo* applicability of this method for enablement purposes.

The specification provides examples wherein antisense compounds targeted to a nucleic acid molecule encoding superoxide dismutase 1 soluble inhibited the expression of superoxide dismutase 1 soluble *in vitro* (cell culture) (see Example 15 and Table 1).

The specification does not demonstrate any correlation with the inhibition of superoxide dismutase 1 soluble in cell culture and inhibiting the expression of superoxide dismutase 1 soluble in any cell or tissue *in vivo* (whole organism). The specification does not present any examples wherein an antisense compound targeted to a nucleic acid molecule encoding superoxide dismutase 1 soluble was delivered to cells *in vivo* (whole organism), nor wherein an antisense compound targeted to a nucleic acid molecule encoding superoxide dismutase 1 soluble inhibited the expression of superoxide dismutase 1 soluble in cells or tissues *in vivo* (whole organism).

At the time the instant invention was made, the therapeutic use of antisense oligonucleotides was highly unpredictable due to obstacles that continue to hinder the therapeutic application of antisense therapy *in vivo* (whole organism) (see for example Agrawal et al. (Molecular Medicine Today, 2000 Vol. 6:72-81), Branch, AD (TIBS, 1998 Vol. 23:45-50) and Jen et al. (Stem Cells, 2000 Vol. 18:307-319)). Such obstacles include, for example, problems with delivery, target accessibility, and the potential for unpredictable nonantisense effects. For example, Jen et al. state, "One of the major limitations for the therapeutic use of AS-ODNs and ribozymes is the problem of delivery... Presently, some success has been achieved in tissue culture, but efficient delivery for *in vivo* animal studies remains questionable" (see page 313, second column, second paragraph). Jen et al. outlines many of the factors limiting the application of antisense for therapeutic purposes and concludes, "Given the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the antisense strategy has proven elusive" (see page 315, second column). Branch

addresses the unpredictability and the problems faced in the antisense art with the following statements: "Antisense molecules and ribozymes capture the imagination with their promise of rational drug design and exquisite specificity. However, they are far more difficult to produce than was originally anticipated, and their ability to eliminate the function of a single gene has never been proven."; "To minimize unwanted non-antisense effects, investigators are searching for antisense compounds and ribozymes whose targets sites are particularly vulnerable to attack. This is a challenging quest."; "However, their unpredictability confounds research application of nucleic acid reagents."; "Non-antisense effects are not the only impediments to rational antisense drug design. The internal structures of target RNAs and their associations with cellular proteins create physical barriers, which render most potential binding sites inaccessible to antisense molecules."; "Years of investigation can be required to figure out what an 'antisense' molecule is actually doing,..."; "Because knowledge of their underlying mechanism is typically acting, non-antisense effects muddy the waters."; "Because biologically active compounds generally have a variety of effects, dose-response curves are always needed to establish a compounds primary pharmacological identity. Antisense compounds are no exception. As is true of all pharmaceuticals, the value of a potential antisense drug can only be judged after its intended clinical use is known, and quantitative information about its dose-response curve of conventional drugs, which typically span two to three orders of magnitude, those of antisense drugs, extend only across a narrow concentration range."; "Because it is very difficult to predict what portions of an RNA molecule will be accessible *in vivo*, effective antisense molecules

must be determined empirically by screening large number of candidates for their ability to act inside cells."; "Binding is the rare exception rather than the rule, and antisense molecules are excluded from most complementary sites. Since accessibility cannot be predicted, rational design of antisense molecules in not possible."; and, "The relationship between accessibility to oligonucleotide (ODN) binding and vulnerability to ODN-mediated antisense inhibition *in vivo* is beginning to be explored...It is not yet clear whether *in vitro* screening techniques...will identify ODNs that are effective *in vivo*."

Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed methods *in vivo*, as broadly claimed. The specification provides examples wherein antisense compounds targeted to a nucleic acid molecule encoding superoxide dismutase 1 soluble are delivered to cells *in vitro* and the expression of superoxide dismutase 1 soluble is inhibited, however, cell culture examples are generally not predictive of *in vivo* inhibition due to differences in metabolites and clearance rates, local concentration of antisense, differences in target site accessibility, cellular uptake differences, and the potential for non-antisense side effects. Often formulations and techniques for delivery *in vitro* (cell culture) are not applicable *in vivo* (whole organism) (see for example Jen et al., page 313, second column, second paragraph). Further, Agrawal et al. (Molecular Medicine Today, 2000, Vol. 6:72-81) (see page 79 and 80, section entitled *Cellular uptake facilitators for in vitro studies*) states, "The cellular uptake of negatively charged oligonucleotides is one of the important factors in determining the efficacy of antisense oligonucleotides... *In vitro*,

cellular uptake of antisense oligonucleotides depends on many factors, including cell type, kinetics of uptake, tissue culture conditions, and chemical nature, length and sequence of the oligonucleotide. Any one of these factors can influence the biological activity of an antisense oligonucleotide". Due to differences in the physiological conditions of a cell *in vitro* versus *in vivo*, the uptake and biological activity observed *in vitro* would not predictably translate to *in vivo* results.

The field of antisense, to date, does not provide guidelines by which antisense can be routinely delivered to generally any cell type *in vivo* (whole organism) at a concentration effective to result in inhibition of gene expression. The specification does not provide specific guidance by which one skilled in the art would expect to be able to deliver an antisense nucleic acid targeted to a nucleic acid molecule encoding superoxide dismutase 1 soluble to generally any target cell or tissue *in vivo* (whole organism) at a concentration effective to inhibit superoxide dismutase 1 soluble gene expression as encompassed by the claims.

In order to practice the invention claimed, over the full scope claimed, one skilled in the art would need to undergo undue trial and error experimentation, beyond the teachings of the instant specification. The quantity of undue experimentation would include the determination of what specific cells or tissues to target with superoxide dismutase 1 soluble antisense compounds and how to specifically deliver antisense compounds to an organism *in vivo* (whole organism) at a concentration effective to result in the inhibition of the expression of superoxide dismutase 1 soluble. Additionally, this undue experimentation would include the determination of such factors as dosage,

route of administration, disposition of the antisense molecule in tissues, and the half-life and stability of the oligonucleotide molecule *in vivo*. Given the art recognized unpredictability of the therapeutic application of antisense *in vivo* (whole organism), this determination would not be routine and would require undue trial and error experimentation.

Therefore, due to the broad scope of the methods claimed, the state of the art of antisense therapy, the level of unpredictability of *in vivo* (whole organism) methods of using antisense, the lack of specific guidance for the *in vivo* (whole organism) application of antisense methods for *in vivo* delivery, and the lack of working examples or examples which correlate with the claimed methods, one skilled in the art would not be able to practice the methods over the full scope claimed without undue trial and error experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 11, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Rothstein et al. (Proc. Natl. Acad. Sci., 1994 Vol. 91:4155-4159, reference AK on Applicant's information disclosure statement filed August 4, 2003).

Claim 1 is drawn to a compound 8 to 50 nucleobases in length targeted to a coding region of a nucleic acid molecule encoding human superoxide dismutase 1 soluble (SEQ ID NO:3), wherein said compound inhibits the expression of superoxide dismutase 1 soluble. Claims 2, 4, and 5 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound is an antisense oligonucleotide; wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage, wherein the modified internucleoside linkage is a phosphorothioate linkage. Claim 11 is drawn to a compound 8 to 50 nucleobases in length which specifically hybridizes with at least an 8-nucleobases portion of an active site on a nucleic acid molecule encoding human superoxide dismutase 1 soluble. Claim 15 is drawn to a method of inhibiting the expression of superoxide dismutase 1 soluble in cells or tissues comprising contacting said cells or tissues (*in vitro*) with the compound of claim 1 so that expression of superoxide dismutase 1 soluble is inhibited.

Rothstein et al. disclose the induction of apoptosis using a 30-mer phosphorothioate antisense oligonucleotide targeting the start codon of human super oxide dismutase 1 soluble in rat spinal cord cultures *in vitro*. It is noted that the 30-mer phosphorothioate antisense oligonucleotide extended from 10 bases upstream of the start codon to 17 bases downstream. Rothstein et al. disclose antisense oligonucleotide treatment produced a long-term 40-55% inhibition of super oxide dismutase 1 activity in organotypic cells in culture (see Figure 2).

Therefore, Rothstein et al. anticipate claim 1, 2, 4, 5, 11, and 15.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rothstein et al. (Proc. Natl. Acad. Sci., 1994 Vol. 91:4155-4159, reference AK on Applicant's information disclosure statement filed August 4, 2003) in view of Baracchini et al. [U.S. Patent No. 5,801,154].

Claim 1 is drawn to a compound 8 to 50 nucleobases in length targeted to a coding region of a nucleic acid molecule encoding human superoxide dismutase 1 soluble (SEQ ID NO:3), wherein said compound inhibits the expression of superoxide dismutase 1 soluble. Claims 2 and 4-10 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound is an antisense oligonucleotide; wherein the antisense oligonucleotide comprises at least one modified

internucleoside linkage, wherein the modified internucleoside linkage is a phosphorothioate linkage, wherein the antisense oligonucleotide comprises at least one modified sugar moiety, wherein the modified sugar moiety is a 2-O-methoxyethyl sugar moiety, wherein the antisense oligonucleotide comprises at least one modified nucleobase, wherein the modified nucleobase is a 5-methylcytosine, wherein the antisense oligonucleotide is a chimeric oligonucleotide. Claim 11 is drawn to a compound 8 to 50 nucleobases in length which specifically hybridizes with at least an 8-nucleobases portion of an active site on a nucleic acid molecule encoding human superoxide dismutase 1 soluble. Claims 12-14 depend from claim 1 and include all the limitations of claim 1 with the further limitations wherein the compound of claim 1 further comprises a pharmaceutical acceptable carrier, diluent, or colloidal dispersion system. Claim 15 is drawn to a method of inhibiting the expression of superoxide dismutase 1 soluble in cells or tissues comprising contacting said cells or tissues with the compound of claim 1 so that expression of superoxide dismutase 1 soluble is inhibited.

Rothstein et al. teach the induction of apoptosis using a 30-mer phosphorothioate antisense oligonucleotide targeting the start codon of human super oxide dismutase 1 soluble in rat spinal cord cultures *in vitro*. It is noted that the 30-mer phosphorothioate antisense oligonucleotide extended from 10 bases upstream of the start codon to 17 bases downstream. Rothstein et al. teach antisense oligonucleotide treatment produced a long-term 40-55% inhibition of super oxide dismutase 1 activity in organotypic cells in culture (see Figure 2).

Rothstein et al. do not teach an antisense oligonucleotide comprising at least one

modified sugar moiety, wherein the modified sugar moiety is a 2-O-methoxyethyl sugar moiety; an antisense oligonucleotide comprising at least one modified nucleobase, wherein the modified nucleobase is a 5-methylcytosine, a chimeric antisense oligonucleotide, or an antisense oligonucleotide comprising a diluent or colloidal dispersion system.

Baracchini et al. teach modified or substituted oligonucleotides are often preferred over native forms because of desirable properties such as enhanced cellular uptake, enhanced affinity for nucleic acid target and increased stability in the presence of nucleases. Baracchini et al. also teach antisense oligonucleotides with at least one modified sugar moiety and a modified 2'-O-methoxyethyl sugar moieties (see Table I)... with modified nucleobases, such as 5-methylcytosine (see column 7, lines 15-25). Baracchini et al. also teach an antisense oligonucleotide as a chimeric oligonucleotide (see column 8, lines 12-19). Baracchini et al. also teach antisense oligonucleotides comprising a diluent or colloidal dispersion system (see column 4, lines 23-36).

It would have been *prima facie* obvious at the time the invention was made for one of ordinary skill in the art to make antisense compounds targeted to superoxide dismutase 1 soluble, including the target sequence of SEQ ID NO:3, using the teachings and motivation of Rothstein et al. and following the method of Baracchini et al.

It would have been obvious to make antisense nucleic acids targeting to superoxide dismutase 1 soluble since Rothstein et al. explicitly teach such. One of ordinary skill in the art would have been motivated to make antisense nucleic acids

targeting to superoxide dismutase 1 soluble since Rothstein et al. teach chronic superoxide dismutase 1 soluble inhibition, using an antisense oligonucleotide, causes apoptotic death of neurons which is important in neurodegenerative disease such as amyotrophic lateral sclerosis.

One of ordinary skill in the art would have had a reasonable expectation of success in making antisense compounds targeted to a nucleic acid molecule encoding superoxide dismutase 1 soluble since Rothstein et al. the design of a 30-mer phosphorothioate antisense oligonucleotide targeting the start codon of human super oxide dismutase 1 soluble. One of ordinary skill in the art would have been motivated to make the antisense compound within the size range of 8 to 50 nucleobases for ease of synthesis and delivery and because it is conventional in the art to make antisense within this size range (as exemplified by Rothstein et al. and Baracchini et al.). One of ordinary skill in the art would have been motivated to target the coding region of a nucleic acid targeted to superoxide dismutase 1 soluble since Rothstein et al. explicitly teach the design of a 30-mer phosphorothioate antisense oligonucleotide targeting the start codon of human super oxide dismutase 1 soluble. One of ordinary skill in the art would have been motivated and had a reasonable expectation of success in modifying the antisense compound since the prior art has taught the desirability of such compounds are often preferred over native forms because of enhanced cellular uptake, enhanced affinity for nucleic acid target, and increased stability (see Baracchini et al.).

It would have been obvious to one of ordinary skill in the art to make a composition comprising a compound targeted to superoxide dismutase 1 soluble and a

pharmaceutically acceptable carrier, including a colloidal dispersion system because pharmaceutically acceptable carriers, including colloidal dispersion systems (e.g. liposomes) were well known in the art for use with antisense molecules as a means to deliver antisense molecules to cells *in vitro* (cell culture), as taught by Baracchini et al. It would have been obvious to one of ordinary skill in the art to use the antisense compound targeting to superoxide dismutase 1 soluble (SEQ ID NO:3) in a method of inhibiting the expression of superoxide dismutase 1 soluble in cells *in vitro* (cell culture) because Rothstein et al. teach such as an obvious use for an antisense molecule targeted to superoxide dismutase 1 soluble.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
October 6, 2005

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